

32. (New) The method according to claim 30, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2.

33. (New) The method according to claim 30, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 3.

34. (New) The method according to claim 30, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 4.

35. (New) The method according to claim 30, wherein the nucleic acid encodes a polypeptide fragment of calpastatin, wherein the fragment inhibits calpain protease activity in cell extracts comprising p53 protein.

36. (New) A composition comprising an adenoviral viral vector and a carrier or excipient suitable for intratumoral delivery, wherein the adenoviral vector comprises a nucleic acid encoding a specific inhibitor of calpain protease activity, wherein the inhibitor is capable of causing a change in the level of detectable p53 protein in a cell or extract of a cell and in the presence of calpain as compared to a control.

37. (New) The composition of claim 36, wherein the nucleic acid comprises the sequence of SEQ ID NO: 1.

38. (New) The composition of claim 36, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2.

39. (New) The composition of claim 36, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 3.

40. (New) The composition of claim 36, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 4.

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41. (New) The composition of claim 36, wherein the nucleic acid encodes a polypeptide fragment of calpastatin, wherein the fragment inhibits calpain protease activity in cell extracts comprising p53 protein.

Remarks

Applicants request entry of the amendments and examination of the application. New claims 30-41 are pending following entry of the amendment. Applicants have amended the claims to reflect the broader aspect of a method or composition for inhibiting protein degradation and/or for specific calpain inhibition, as disclosed at page 4, line 21, through page 7, line 20. No new matter enters by the amendments.

Initially, applicants wish to point out that applicants were the first to identify the importance calpain-dependent degradation has on cellular p53 levels and to show how these levels can be manipulated by inhibitors of calpain activity. The Pariat *et al.* document, submitted herewith, discusses the role of calpain in p53 degradation. The document shows that, as described in applicants' specification, p53 levels can be altered through the manipulation of calpain activity (*see*, for example, pages 2811 and 2812, where the expression of calpastatin influences both transcription and p53 protein levels). The difference in expression systems used, Pariat *et al.* referring to a plasmid system while the applicants' Example 4 refers to an adenoviral system, would not lead one of skill in the art to question the correlation between the findings and applicants' assertions in the specification. In fact, applicants disclose several possible expression and delivery systems (*see* page 9 of the specification).